



NOTES

COCCOBACILLI: FACULTATIVE ANAEROBES

MICROBE OVERVIEW

- Intermediate shape between cocci (spherical bacteria), bacilli (rod-shaped bacteria)
- Gram-negative, facultative anaerobes, nonmotile, nonspore-forming

BRUCELLA

osms.it/brucella

PATHOLOGY & CAUSES

- Characteristics
 - Zoonotic infection
 - Urease, catalase positive
 - Facultatively intracellular
 - Sensitive to heat, ionizing radiation, disinfectants, pasteurization
- Virulence factors
 - Lipopolysaccharide (LPS): promotes cell entry, evasion, intracellular killing
 - Type IV secretion system (key virulence factor): injection of effector molecules into host cell → modifies endoplasmic reticulum, enables replication
- Culture
 - Isolation specimen: blood, bone marrow, body fluids, tissues
 - Media: biphasic (solid, liquid) Ruiz-Castaneda blood culture/modern automated blood culture systems (faster, more effective)
 - Raised, convex colonies with smooth, shiny surface
- Causative agent of brucellosis
- Most common zoonotic infection to cause disease in humans

Transmission

- Contact with infected animals (e.g. sheep, cattle, goats, pigs, etc)
 - Entry of bacteria through skin lesions, conjunctival inoculation, inhalation of contaminated aerosol
- Ingestion of contaminated animal products (e.g. unpasteurized milk, cheese; undercooked meat)
 - Remains viable up to two days in milk at 8°C/46.4°F, three weeks in frozen meat, three months in goat cheese

Pathogenesis

- Inoculation of bacteria → ingestion by polymorphonuclears, macrophages → passage to local lymph nodes → bacteria replicates intracellularly → some bacteria avoid intracellular killing by different strategies (e.g. inducing phagocyte apoptosis, inhibiting phagocyte-lysosome fusion) → chronic infection

TYPES

Acute infection

- Localized infection (30% of cases), can affect any organ

VISIT...

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- **Skeletal** (most common): arthritis, spondylitis, sacroiliitis, osteomyelitis
- **Pulmonary**: bronchitis, interstitial pneumonitis, lobar pneumonia, pulmonary nodules, pleural effusion, empyema, abscesses
- **Cardiac**: endocarditis, myocarditis, pericarditis, endarteritis
- **Alimentary**: cholecystitis, ileitis, colitis, pancreatitis
- **Reticuloendothelial**: reactive hepatitis, granulomas, acute hepatitis with focal necrosis (*B. melitensis*), formation of noncaseating sarcoidosis-like granulomas (*B. abortus*), suppurative abscess formation (*B. suis*) in liver
- **Genitourinary**: orchitis, epididymitis
- **Hematological**: anemia, leukopenia, thrombocytopenia, pancytopenia, disseminated intravascular coagulation
- **Neurologic**: meningitis, encephalitis, myelitis, radiculitis, neuritis, mycotic aneurysms, brain abscess
- **Ocular**: uveitis, keratoconjunctivitis, corneal ulcers, iridocyclitis, nummular keratitis, choroiditis, optic neuritis, papilledema, endophthalmitis
- **Dermatologic**: nonspecific skin eruptions, ulcerations, petechiae, purpura, granulomatous vasculitis, abscesses

Chronic infection

- Symptoms persist one year after diagnosis; localized infection, relapse

RISK FACTORS

- Occupational exposure
 - Lab health care workers, farmers, slaughterhouse workers, veterinarians

COMPLICATIONS

- Infection during pregnancy → intrauterine infection, premature delivery, spontaneous abortion, miscarriage
- Endocarditis damage, destroy heart valves
- Leading cause of death by brucellosis
- Skeletal
 - May cause long-term damage, bone/joint malformations
- Neurologic
 - May lead to permanent brain damage
- Ocular
 - Visual impairment

BRUCELLA OVERVIEW

	NATURAL HOST	PATHOLOGY
B. abortus	Cattle	Liver, spleen commonly affected; causes sarcoidosis-like granulomas in liver
B. canis	Dogs	Rare, causes mild disease
B. melitensis	Small ruminants (goats, sheep)	Causes severe disease, fevers of unknown origin, hepatosplenomegaly, pancytopenia
B. suis	Swine, rodents	Causes suppurative abscess formation in liver

SIGNS & SYMPTOMS

- Range from asymptomatic to severe illness
- Onset of symptoms can be acute/insidious
- Incubation
 - 1–4 weeks to several months
- Acute generalized infection
 - Acute **undulating fever** (key sign), arthralgia, myalgia, fatigue, headache, night sweats, malaise, weight loss
 - Hepatomegaly, splenomegaly, lymphadenopathy
 - Foul-smelling perspiration (characteristic sign)
- Localized infection
 - Symptoms depend on organ/organ system affected

DIAGNOSIS

LAB RESULTS

- Rising titers of specific antibodies
 - Initial rise in IgM class titers, followed in several weeks by predominance of IgG antibodies; both decrease over time with treatment
- Anemia, thrombocytopenia

Microbe identification

- Positive bodily fluids/tissue culture
- Serum agglutination, enzyme-linked immunosorbent assay (ELISA)
- Polymerase chain reaction (PCR)

- Lysis-centrifugation technique

OTHER DIAGNOSTICS

- History of travel, food consumption, occupation

TREATMENT

MEDICATIONS

- Six-week course of doxycycline plus streptomycin/gentamicin/doxycycline plus rifampin
- In children < eight years old
 - Trimethoprim-sulfamethoxazole (TMP-SMX) plus rifampin

SURGERY

- Surgical interventions sometimes necessary for osteoarticular manifestations (e.g. pyogenic joint effusions), hepatosplenic granulomas/abscesses, cardiac complications (e.g. valve replacement surgery)

OTHER INTERVENTIONS

- Prophylaxis
 - Biosafety level 3 in laboratories recommended while handling *Brucella* cultures
 - No vaccines for humans; live attenuated vaccines containing strains of *B. abortus*, *B. melitensis* used for animals

HAEMOPHILUS DUCREYI

osms.it/haemophilus-ducreyi

PATHOLOGY & CAUSES

- Virulence factors
 - Lipooligosaccharide
 - *Pili*: provides attachment of bacteria
 - Soluble cytolethal distending toxin, cytotoxic hemolysin, hemoglobin-binding protein, copper-zinc superoxide dismutase, filamentous hemagglutinin-like protein, zinc-binding periplasmic protein
- Culture
 - *Isolation specimen*: genital ulcer swab, lymph node aspirate
 - *Media*: enriched growth medium contains factor X (hemin), serum incubated at 33–35°C/91.4–95°F with CO₂; small, heterogenous, gray/translucent colonies
- Causative agent of sexually transmitted genital ulcer called **chancroid** (AKA *ulcus molle*), associated inguinal lymphadenopathy
- Some strains causes cutaneous ulcers in children in South Pacific, parts of equatorial Africa

Transmission

- Sexual intercourse (genital ulcers)
- Nonsexual transmission (cutaneous ulcers)

Pathogenesis

- Incubation
 - 4–10 days
- Inoculation through epidermal microabrasions → attachment of bacteria to extracellular matrix in skin via pili,

lipooligosaccharide → attachment to cells via specific heat shock protein (GroEL) → cytotoxin release, epithelial injury → formation of erythematous papule → evolves into pustule → pustule ruptures, forms ulcer

RISK FACTORS

- Uncircumcised individuals, poverty, multiple sexual partners

COMPLICATIONS

- Increases risk for HIV contraction

SIGNS & SYMPTOMS

- Single/multiple **painful genital ulcers** on erythematous base, 1–2cm/0.39–0.79in diameter with sharply demarcated borders; base of ulcer covered with purulent **exudate**, bleeds easily when scraped
- Predilection sites
 - Prepuce, coronal sulcus, glans penis in individuals who are biologically male
 - Labia, vaginal introitus, perianal area in individuals who are biologically female
- Individuals who are biologically female
 - Dysuria, dyspareunia, vaginal discharge, rectal bleeding, painful defecation
- **Inguinal lymphadenopathy** in approx. 50% of cases (more common in individuals who are biologically male)
 - Painful fluctuant buboes (swollen lymph nodes); if untreated, may spontaneously rupture, form draining sinus, releases pus

DIAGNOSIS

LAB RESULTS

Microbe identification

- Diagnosis of confirmed chancroid
 - Culture (not widely available)
- Nucleic acid amplification tests
 - Not available outside of clinical research purposes
- Polymerase chain reaction (PCR) multiplex
 - Detection of bacterial DNA
- Histologic characteristics of chancroid

OTHER DIAGNOSTICS

- Diagnostic criteria for probable chancroid
 - ≥ one painful genital ulcers
 - No evidence of *Treponema pallidum* infection (by darkfield microscopy/serologic testing)
 - No evidence of *Herpes simplex virus* (HSV) infection
 - Appearance of genital ulcers, regional lymphadenopathy
- Purulent exudate in superficial epidermis with perivascular, interstitial mononuclear infiltrate in dermis



Figure 64.1 An ulcer on the glans penis of a male with chancroid. The ulcer is typically painful, unlike the ulcer of primary syphilis.

TREATMENT

MEDICATIONS

- Single-dose therapy with azithromycin/ceftriaxone
- Alternative
 - Multiple-dose therapy with ciprofloxacin/erythromycin

OTHER INTERVENTIONS

- Fluctuant lymphadenopathy
 - Needle aspiration, drainage to prevent spontaneous rupture

HAEMOPHILUS INFLUENZAE

osms.it/haemophilus-influenzae

PATHOLOGY & CAUSES

- **Haemophilus:** blood loving
- Characteristics
 - Catalase, oxidase positive
- Virulence factors
 - **Polysaccharide capsule:** prevents phagocytosis; causes ciliostasis, evades mucociliary clearance of bacteria; classified into six serotypes based on capsular antigens (A, B, C, D, E, F); some strains unencapsulated (AKA nontypable); most clinical isolates *Haemophilus influenzae* type B (Hib)/nontypable
 - IgA1 protease, adherence factors, antigenic variation, biofilm formation
- Gram stain of exudate shows bacteria arranged in chains ("school of fish")
- Culture
 - **Isolation specimen:** cerebrospinal fluid (CSF), urine, serum, synovial fluid
 - **Media:** chocolate agar/Fildes medium (hemolyzed erythrocytes) with factor X (hemin), V (nicotinamide adenine dinucleotide) supplementation in aerobic, only factor X supplementation in anaerobic environment
 - Convex, smooth, grey/transparent colonies
- Gram-negative coccobacillus → meningitis, respiratory tract infections
- Nontypeable strains colonize nasopharynx of 40–80% children, adults
- Hib colonizes 3–5% children

TYPES

Hib

- Epiglottitis in older children, adults
- Cellulitis (most common in young children)
- Pneumonia
 - Sometimes with meningitis, epiglottitis
- Meningitis, septic arthritis, osteomyelitis

Nontypable

- Less invasive due to lack of capsule; causes mild localized respiratory tract disease in children, adults
- More severe in immunocompromised/predisposed individuals
 - Otitis media, sinusitis, purulent conjunctivitis, bacterial pneumonia in children (in low-income countries), neonatal bacteremia
 - Community-acquired pneumonia in adults with underlying lung disease
 - Exacerbation of chronic obstructive pulmonary disease (COPD)
 - Meningitis in individuals with predisposition/conditions causing leakage of CSF fluid (e.g. sinusitis, otitis media, head trauma)

Transmission

- Direct contact with respiratory tract secretions/airborne respiratory droplets

Pathogenesis

- Inoculation → passage through upper respiratory tract → adherence to respiratory epithelium, LPS inhibits mucociliary clearance → colonization spreads throughout respiratory tract → sinuses, otitis, pneumonia
- IgA1 protease, antigenic variation, paracytosis, biofilm formation → perseverance of bacteria

RISK FACTORS

- Viral infection, sickle-cell disease, asplenia, HIV infection, malignancies, congenital deficiencies of complement components

COMPLICATIONS

- Nontypable in neonates, immunocompromised individuals → septicemia, meningitis, septic arthritis
- Hib meningitis → subdural effusion/empyema; ischemic/hemorrhagic cortical

infarction; cerebritis (nonviral parenchymal infection of brain); ventriculitis; intracerebral abscess; hydrocephalus; neurologic sequelae (e.g. permanent sensorineural hearing loss, seizures, intellectual disability)

- Hib pneumonia can spread to pericardium → purulent pericarditis

SIGNS & SYMPTOMS

Hib

- **Meningitis**
 - Fever, lethargy, irritability, vomiting, altered mental status
 - Fulminant course → rapid neurologic deterioration, respiratory arrest
 - **Positive Kernig's sign:** inability to straighten leg when hip flexed to 90°
 - **Positive Brudzinski's sign:** flexing of neck by examiner → flexing of hips, knees
- **Epiglottitis**
 - Fever, sore throat, difficulty speaking, dyspnea → severe stridor, dysphagia, pooling of secretions, drooling
 - **"Tripod" posture:** individual takes sitting position with trunk leaning forward, neck hyperextended, chin thrust forward to get more air through obstructed airway
- **Cellulitis**
 - Fever; warm, tender area of erythema/violaceous discoloration on cheek/periorbital area
- **Septic arthritis**
 - Fever, pain, swelling, tenderness, decreased mobility of affected joint

Nontypeable

- **Otitis media**
 - Fever, ear pain, irritability, sleep disturbance, otorrhea
 - Red bulging tympanic membrane with decreased mobility upon pneumatic otoscopy examination
 - Often conjoined with conjunctivitis
- **Sinusitis**
 - Fever, persistent purulent nasal discharge or cough > 10 days
 - Tenderness over involved paranasal sinuses

DIAGNOSIS

DIAGNOSTIC IMAGING

Laryngoscopy

- Red, swollen epiglottis; aryepiglottic folds
- Examine with caution; possible laryngeal spasm

X-ray

- **Thumb sign on epiglottis** (radiographic corollary of omega sign)

LAB RESULTS

Microbe identification

- Positive Gram stain, bacterial culture of CSF, synovial fluid, epiglottis, pleural, pericardial, other sterile fluids
- Latex agglutination, enzyme immunoassay, coagglutination
 - Type B capsular antigen detection in CSF, serum, urine
- Definitive diagnosis
 - Culture of fluid obtained by sinus aspiration, tympanocentesis, tracheal/lung aspiration, bronchoscopy, bronchoalveolar lavage



Figure 64.2 An X-ray image of the chest demonstrating diffuse airway shadows in an individual with bronchopneumonia. *H. influenzae* is a causative organism of bronchopneumonia.

TREATMENT

MEDICATIONS

Prevention

- Conjugate Hib vaccines
 - Routine vaccination of infants of two months
- Rifampin chemoprophylaxis
 - Individuals in close contact with infected; incompletely vaccinated individuals in households with infants/children < four years old

Hib with meningitis

- Third generation cephalosporins
 - **Adults:** **ceftriaxone**

- **Children:** **ceftriaxone** plus dexamethasone (decreases immune response to released LPS upon bacterial death, lowers chance for destruction of neurons, neurologic sequelae)

- Epiglottitis (life-threatening condition; prompt treatment paramount)
 - **Ceftriaxone**

Nontypable

- **Amoxicillin/clavulanate**, broad-spectrum cephalosporins, macrolides (azithromycin/clarithromycin), fluoroquinolones

SURGERY

- Epiglottitis
 - Placement of artificial airway

PASTEURELLA MULTOCIDA

osms.it/pasteurella-multocida

PATHOLOGY & CAUSES

- Characteristics
 - Zoonotic infection (e.g. birds, cats, dogs, rabbits, cattle, pigs); oxidase, catalase, nitrate reduction positive
- Virulence factors
 - **Polysaccharide capsule:** prevents phagocytosis; divided into serogroups based on capsular antigens (A, B, C, D, E)
 - **Lipopolysaccharide:** endotoxin
 - Sialidases, hyaluronidase, surface adhesins, iron acquisition proteins, pasteurella multocida toxin (PMT)
- Culture
 - **Isolation specimen:** respiratory tract samples, CSF
 - **Media:** sheep blood, chocolate, HS, Mueller–Hinton agar at 37°C/98.6°F; opaque/gray colonies 1–2mm in diameter
- Medically important subspecies
 - *P. multocida* subsp *multocida*, *P.*

multocida subsp *septica*, *P. multocida* subsp *gallicida*

Transmission

- Most commonly **cat/dog bites**, scratches, licks

TYPES

- Soft tissue infections
 - **Cellulitis at site of inoculation** (most common) → abscess, necrotizing soft tissue infections, septic arthritis, **osteomyelitis**
- Respiratory infections
 - Due to underlying chronic pulmonary disease; glossitis, pharyngitis, sinusitis, otitis media, epiglottitis, tracheobronchitis, pneumonia, empyema, lung abscess
- Invasive infection (immunocompromised, infants)
 - Bacteremia, meningitis, intra-abdominal infections (peritonitis, appendicitis), endocarditis, septic arthritis, ocular infection

Pathogenesis

- Inoculation → attachment of bacteria to ECM, cells soft tissue → PMT secretion → tissue inflammation within 24 hours

COMPLICATIONS

- Sepsis, septic shock

SIGNS & SYMPTOMS

- Soft tissue infections
 - Wound inflammation, cellulitis with purulent drainage; regional lymphadenopathy
- Respiratory tract infections
 - Fever, malaise, dyspnea, pleuritic chest pain
- Sepsis
 - Purpura fulminans (rash rapidly progresses from petechiae, purpura to gangrene/limb amputation)
- Respiratory infection
 - Wheezing, rhonchi, dullness

DIAGNOSIS**LAB RESULTS****Microbe identification**

- Culture, PCR, serological testing

OTHER DIAGNOSTICS

- History of animal contact
 - Cat bites pose higher risk for developing osteomyelitis, septic arthritis

TREATMENT**MEDICATIONS**

- Penicillins
- Tetracyclines
- Cephalosporins
- Quinolones